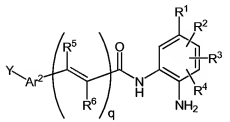
Amendments to the Claims

The following listing of claims will replace all prior versions and listings of claims in the application.

Listing of Claims:

1. (Currently amended) A histone deacetylase inhibitor of formula (1):



(1)

or a pharmaceutically acceptable salt thereof, wherein

Ar^2 is a saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly-cyclic hydrocarbyl, optionally containing one, two, three, or four annular heteroatoms per ring optionally substituted with one or more groups selected from C_1-C_7-alkyl, hydroxy, C_1-C_7-alkoxy, halo, and amino, provided that an annular O or S is not adjacent to another annular O or S;

R^5 and R^6 are independently selected from the group consisting of hydrogen, C_1-C_7-alkyl, aryl, and aralkyl;

R^2, R^3 and R^4 are independently selected from the group consisting of hydrogen, halogen, $-NH_2$, nitro, hydroxy, aryl, heterocyclyl, C_3-C_8-cycloalkyl, heteroaryl, C_1-C_7-akyl, haloalkyl, C_1-C_7-alkenyl, C_1-C_7-alkynyl, C_1-C_7-acyl, C_1-C_7-alkyl-aryloxy, C_1-C_7-alkyl-arylsulfanyl, C_1-C_7-alkyl-arylsulfinyl, C_1-C_7-alkyl-arylsulfonyl, C_1-C_7-alkyl-arylaminosulfonyl, C_1-C_7-alkyl-arylamine, C_1-C_7-alkynyl-C(O)-amine, C_1-C_7-alkenyl-C(O)-amine, C_1-C_7-alkynyl-R^9, C_1-C_7-alkenyl-R^9 wherein R^9 is hydrogen , hydroxy, amino, C_1-C_7-alkyl or C_1-C_7-alkoxy;

q is 0 or 1;

R^1 is a mono-, bi-, or tri-cyclic aryl or heteroaryl, each of which is optionally substituted;

Y is Cy^2-X^1- and

~~Cy^2 is hydrogen, cycloalkyl, aryl, heteroaryl, or heterocyclyl, each of which is optionally substituted and each of which is optionally fused to one or two aryl or heteroaryl rings, or to one or two saturated or partially unsaturated cycloalkyl or heterocyclic rings, and wherein any of the aforementioned rings are optionally substituted; and~~

~~X^1 is selected from the group consisting of a covalent bond, M^1-L^2-M^1, and L^2-M^2-L^2 wherein~~

~~L^2, at each occurrence, is independently selected from the group consisting of a chemical bond, C_0-C_4-hydrocarbyl, C_0-C_4-hydrocarbyl-(NH)-C_0-C_4-hydrocarbyl, C_0-C_4-hydrocarbyl-(S)-C_0-C_4-hydrocarbyl, and C_0-C_4-hydrocarbyl-(O)-C_0-C_4-hydrocarbyl, provided that L^2 is not a chemical bond when X^1 is M^1-L^2-M^1;~~

~~M^1, at each occurrence, is independently selected from the group consisting of -O-, -N(R^7)-, -S-, -S(O)-, -S(O)$_2$-, -S(O)$_2$N(R^7)-, -N(R^7)-S(O)$_2$-, -C(O)-, -C(O)-NH-, -NH-C(O)-, -NH-C(O)-O- and -O-C(O)-NH-, -NH-C(O)-NH-,~~

~~R^7 is selected from the group consisting of hydrogen, C_1-C_6-hydrocarbyl, aryl, aralkyl, acyl, C_0-C_6-hydrocarbyl-heterocyclyl, and C_0-C_6-hydrocarbyl-heteroaryl, wherein the hydrocarbyl moieties are optionally substituted with -OH, -NH$_2$, -N(H)CH$_3$, -N(CH$_3$)$_2$, or halo; and~~

~~M^2 is selected from the group consisting of M^1, heteroarylene, and heterocyclylene, either of which rings optionally is substituted~~~~Y is Cy^2-X^1-~~ and

Cy^2 is hydrogen, cycloalkyl, aryl, heteroaryl, or heterocyclyl, each of which is optionally substituted and each of which is optionally fused to one or two aryl or heteroaryl rings, or to one or two saturated or partially unsaturated cycloalkyl or heterocyclic rings, and wherein any of the aforementioned rings are optionally substituted; and

X^1 is selected from the group consisting of a covalent bond, M^1-L^2-M^1, and L^2-M^2-L^2 wherein

L^2, at each occurrence, is independently selected from the group consisting of a chemical bond, C_0-C_4-hydrocarbyl, C_0-C_4-hydrocarbyl-(NH)-C_0-C_4-

hydrocarbyl, C_0-C_4-hydrocarbyl-(S)-C_0-C_4-hydrocarbyl, and C_0-C_4-hydrocarbyl-(O)-C_0-C_4-hydrocarbyl, provided that L^2 is not a chemical bond when X^1 is M^1-L^2-M^1;

M^1, at each occurrence, is independently selected from the group consisting of -O-, -N(R^7)-, -S-, -S(O)-, S(O)$_2$-, -S(O)$_2$N(R^7)-, -N(R^7)-S(O)$_2$-, -C(O)-, -C(O)-NH-, –NH-C(O)-, -NH-C(O)-O--and -O-C(O)-NH-, -NH-C(O)-NH-,

R^7 is selected from the group consisting of hydrogen, C_1-C_6-hydrocarbyl, aryl, aralkyl, acyl, C_0-C_6-hydrocarbyl-heterocyclyl, and C_0-C_6-hydrocarbyl-heteroaryl, wherein the hydrocarbyl moieties are optionally substituted with –OH, -NH_2, -N(H)CH_3, –N(CH_3)$_2$, or halo; and

M^2 is selected from the group consisting of M^1, heteroarylene, and heterocyclylene, either of which rings optionally is substituted; and

provided that

when R^1 is *N*-imidazolyl, R^2-R^4 are H, q is 0, and Ar^2 is pyridine, Y is not Cl; and

when R^1 is *p*-aminophenyl, R^2-R^4 are H, q is 0, and Ar^2 is phenyl, Y is not H.

2. (Original) The compound according to claim 1 wherein R^1 is phenyl, naphthyl, anthracenyl, or fluorenyl.

3. (Original) The compound according to claim 1 wherein R^1 is furanyl or thienyl.

4. (Original) The compound according to claim 2 wherein R^2, R^3, and R^4 are all –H.

5. (Original) The compound according to claim 3 wherein R^2, R^3, and R^4 are all –H.

6. (Canceled)

7. (Previously presented) The compound according to claim 1, wherein X^1 is selected from the group consisting of a -N(Z)-C_0-C_7-alkyl-, -O-C_0-C_7-alkyl-, -C(H)=CH-C_0-C_7-alkyl-, -S-C_0-C_7-alkyl-, or -C_1-C_7-alkyl-, wherein Z is -H or -C_1-C_7-alkyl- optionally substituted with -OH, -NH_2, or halo.

8. (Previously presented) The compound according to claim 1, wherein X^1 is selected from methylene, aminomethyl, and thiomethyl.

9. (Previously presented) The compound according to claim 1, wherein Cy^2 is selected from








, and

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each of which optionally is substituted and optionally is fused to one or more aryl rings.

10. (Previously presented) The compound according to claim 1 wherein Cy^2 is aryl or heteroaryl, each optionally substituted.

11. (Previously presented) The compound according to claim 1 wherein Cy^2 is phenyl, pyrimidinyl, benzoimidazolyl or benzothiazolyl, each of which is optionally substituted.

12. (Original) The compound according to claim 11 wherein Cy^2 has from one and three substituents independently selected from the group consisting of C_1-C_7-alkoxy, halo, di-C_1-C_7-alkylamino-C_1-C_7-alkoxy and heteroaryl.

13. (Original) The compound according to claim 12 wherein the substituents are selected from methoxy, fluoro, chloro, pyridinyl and dimethylamino-ethoxy.

14. (Original) The compound according to claim 13 wherein Cy^2 is phenyl substituted with one to three CH_3O-.

15. (Previously presented) The compound according to claim 1 wherein Y is $(V'\text{-}L^4)_t\text{-}V\text{-}L^3$-, and

L^3 is a direct bond, -C_1-C_6-hydrocarbyl, -$(C_1$-C_3-hydrocarbyl$)_{m1}$-X'-$(C_1$-C_3-hydrocarbyl$)_{m2}$, -NH-(C_0-C_3-hydrocarbyl), (C_1-C_3- hydrocarbyl)-NH-, or -NH-(C_1-C_3-hydrocarbyl)-NH-;

m1 and m2 are independently 0 or 1;

X' is -$N(R^{21})$-, -$C(O)N(R^{21})$-, $N(R^{21})C(O)$-, -O-, or -S-;

R^{21} is -H, V"-(C_1-C_6-hydrocarbyl)$_a$;

L^4 is (C_1-C_6-hydrocarbyl)$_a$-M-(C_1-C_6-hydrocarbyl)$_b$;

a and b are independently 0 or 1;

M is -NH-, -NHC(O)-, -C(O)NH-, -C(O)-, -SO_2-, -$NHSO_2$-, or -$S0_2$NH-

V, V', and V" are independently selected from cycloalkyl, heterocyclyl, aryl, and heteroaryl;

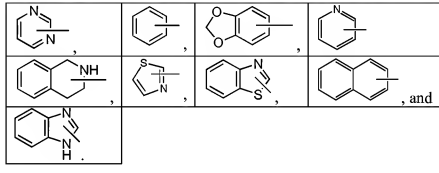
t is 0 or 1.

16. (Original) The compound according to claim 15 wherein Y is V-L^3 and

L^3 is -NH-CH- or –CH-NH-;

V is phenyl optionally substituted with from 1 to 3 moieties independently selected from halo, hydroxy, C_1-C_6-hydrocarbyl, C_1-C_6-hydrocarbyl-oxy or -thio (particularly methoxy or methylthio), wherein each of the hydrocarbyl moieties are optionally substituted with one or more moieties independently selected from halo, nitroso, amino, sulfonamido, and cyano.

17. (Original) The compound according to claim 16 wherein V is an optionally substituted ring moiety selected from:



18. (Previously presented) The compound according to claim 1 wherein

Cy^2 is cycloalkyl, aryl, heteroaryl, or heterocyclyl, each of which optionally is substituted, and each of which optionally is fused to one or more aryl or heteroaryl rings, or to one or more saturated or partially unsaturated cycloalkyl or heterocyclic rings, each of which rings optionally is substituted, provided that when Cy^2 is a cyclic moiety having -C(O)-, -C(S)-, -S(O)-, or -$S(O)_2$- in the ring, then Cy^2 is not additionally substituted with a group comprising an aryl or heteroaryl ring; and

X^1 is selected from the group consisting of a chemical bond, L^3, W^1-L^3, L^3-W^1, W^1-L^3-W^1, and L^3-W^1-L^3, wherein

W^1, at each occurrence, is S, O, or $N(R^9)$, where R^9 is selected from the group consisting of hydrogen, alkyl, aryl, and aralkyl; and

L^3 is C_1-C_4 alkylene, C_2-C_4 alkenylene, or C_2-C_4 alkynylene.

19. (Previously presented) The compound according to claim 1 wherein Y is selected from:

a) A_1-L_1-B_1-, wherein A_1 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_1 is $-(CH_2)_{0-1}NH(CH_2)_{0-1}$-, -NHC(O)-, or $-NHCH_2$-; and wherein B_1 is phenyl or a covalent bond;

b) A_2-L_2-B_2-, wherein A_2 is $CH_3(C{=}CH_2)$-, optionally substituted cycloalkyl, optionally substituted alkyl, or optionally substituted aryl; wherein L_2 is –C≡C-; and wherein B_2 is a covalent bond;

c) A_3-L_3-B_3-, wherein A_3 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_3 is a covalent bond; and wherein B_3 is $–CH_2NH$-;

d) A_4-L_4-B_4-, wherein A_4 is an optionally substituted aryl; wherein L_4 is $–NHCH_2$-; and wherein B_4 is a thienyl group;

e) A_5-L_5-B_5-, wherein A_5 is an optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_5 is a covalent bond; and wherein B_5 is $-SCH_2$-;

f) morpholinyl-CH_2-

g) optionally substituted aryl;

h) A_6-L_6-B_6-, wherein A_6 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_6 is a covalent bond; and wherein B_6 is $–NHCH_2$-;

i) A_7-L_7-B_7-, wherein A_7 is an optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_7 is a covalent bond; and wherein B_7 is $–CH_2$-;

j) optionally substituted heteroaryl or optionally substituted heterocyclyl;

k) A_8-L_8-B_8-, wherein A_8 is optionally substituted phenyl; wherein L_8 is a covalent bond; and wherein B_8 is –O-;

l) A_9-L_9-B_9-, wherein A_9 is an optionally substituted aryl; wherein L_9 is a covalent bond; and wherein B_9 is a furan group;

m) A_{10}-L_{10}-B_{10}-, wherein A_{10} is an optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{10} is $-CH(CH_2CH_3)-$; and wherein B_{10} is $-NHCH_2-$;

n) A_{11}-L_{11}-B_{11}-, wherein A_{11} is an optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{11} is a covalent bond; and wherein B_{11} is $-OCH_2-$;

o) A_{12}-L_{12}-B_{12}-, wherein A_{12} is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{12} is-NHC(O)-; and wherein B_{12} is –N(optionally substituted aryl)CH_2-;

p) A_{13}-L_{13}-B_{13}-, wherein A_{13} is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{13} is a covalent bond; and wherein B_{13} is -NHC(O)-;

q) A_{14}-L_{14}-B_{14}-, wherein A_{14} is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{14} is-NHC(O)(optionally substituted heteroaryl); and wherein B_{14} is –S-S-;

r) $F_3CC(O)NH$-;

s) A_{15}-L_{15}-B_{15}-, wherein A_{15} is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{15} is-$(CH_2)_0$-$_1$NH(optionally substituted heteroaryl)-; and wherein B_{15} is $-NHCH_2-$;

t) A_{16}-L_{16}-B_{16}-, wherein A_{16} is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{16} is a covalent bond; and wherein B_{16} is –N(optionally substituted alkyl)CH_2-; and

u) A_{17}-L_{17}-B_{17}-, wherein A_{17} is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein L_{17} is a covalent bond; and wherein B_{17} is –(optionally substituted aryl-$CH_2)_2$-N-.

20. (Previously presented) The compound according to claim 1 wherein Y is selected from:

a) D_1-E_1-F_1-, wherein D_1 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein E_1 is $-CH_2-$ or a covalent bond; and wherein F_1 is a covalent bond;

b) D_2-E_2-F_2-, wherein D_2 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein E_2 is $-NH(CH_2)_{0-2}-$; and wherein F_2 is a covalent bond;

c) D_3-E_3-F_3-, wherein D_3 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein E_3 is $-(CH_2)_{0-2}NH-$; and wherein F_3 is a covalent bond;

d) D_4-E_4-F_4-, wherein D_4 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein E_4 is $-S(CH_2)_{0-2}-$; and wherein F_4 is a covalent bond;

e) D_5-E_5-F_5-, wherein D_5 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein E_5 is $-(CH_2)_{0-2}S-$; and wherein F_5 is a covalent bond; and

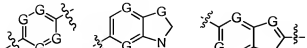
f) D_6-E_6-F_6-, wherein D_6 is an optionally substituted aryl, optionally substituted heteroaryl or optionally substituted heterocyclyl; wherein E_6 is $-NH(CH_2)_{0-2}NH-$; and wherein F_6 is a covalent bond.

21. (Original) The compound according to claim 2 wherein R^2 to R^4 are independently hydrogen, $-NH_2$, nitro, furanyl, chloro, fluoro, butyl, trifluoromethyl, bromo, thienyl, phenyl, $-CHCHC(O)-NH_2$, $-C\equiv CCH_2-R^9$ wherein R^9 is hydrogen, C_1-C_7-alkyl, hydroxy, amino, or C_1-C_7-alkoxy.

22. (Original) The compound according to claim 3 wherein R^2 to R^4 are independently hydrogen, $-NH_2$, nitro, furanyl, chloro, fluoro, butyl, trifluoromethyl, bromo, thienyl, phenyl, $-CHCHC(O)-NH_2$, $-C\equiv CCH_2-R^9$ wherein R^9 is hydrogen, C_1-C_7-alkyl, hydroxy, amino, or C_1-C_7-alkoxy.

23. (Previously presented) The compound according to claim 1 wherein q is 0 and X^1 is independently selected from the group consisting of a $-NH-CH_2-$, $-S-CH_2-$ and $-CH_2-$.

24. (Original) The compound according to claim 1 wherein Ar^2 has the formula



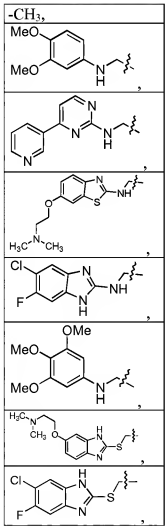
, , or

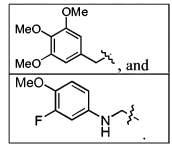
and wherein G, at each occurrence, is independently N or C, and C is optionally substituted.

25. (Original) The compound according to claim 24 wherein Ar^2 has the formula

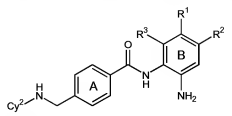
26. (Original) The compound according to claim 24 wherein Ar^2 is selected from the group consisting of phenylene, benzofuranylene and indolinylene.

27. (Previously presented) The compound according to claim 1 wherein the moiety formed by Cy^2-X^1 is selected from:





28. (Previously presented) The compound of claim 1 of formula (2):



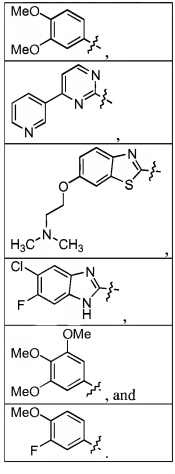
(2)

or a pharmaceutically acceptable salt thereof, wherein

R^2 and R^3 are independently selected from the group consisting of hydrogen, trifluoromethyl, butyl, $-(CH_2)_3$-OH, chloro, fluoro, amino, phenyl, thienyl, furanyl, -CHCCHC(O)NH_2, $-C{\equiv}CCH_2$-OH, $-C{\equiv}CCH_2OCH_3$; and

the A ring is optionally further substituted with from 1 to 3 substituents independently selected from methyl, hydroxy, methoxy, halo, and amino.

29. (Original) The compound according to claim 28 wherein Cy^2 is selected from:



30. (Original) The compound according to claim 28 wherein the A ring is not further substituted.

31. (Original) The compound according to claim 28 wherein R^2 and R^3 are -H.

32. (Original) A compound according to claim 1 selected from:

N-[2-amino-5-(2-thienyl)phenyl]-4-{[(3,4-dimethoxyphenyl)amino]methyl}benzamide;

N-[2-amino-5-(2-thienyl)phenyl]-4-{[(4-pyridin-3-ylpyrimidin-2-yl)amino]methyl}benzamide;

N-[2-amino-5-(2-thienyl)phenyl]-4-[({6-[2-(dimethylamino)ethoxy]-1*H*-benzimidazol-2-yl}thio)methyl]benzamide;

N-[2-amino-5-(2-thienyl)phenyl]-4-{[(5-chloro-6-fluoro-1*H*-benzimidazol-2-yl)amino]methyl}benzamide;

N-[2-amino-5-(2-thienyl)phenyl]-5-{[(3,4,5-trimethoxyphenyl)amino]methyl}-1-benzofuran-2-carboxamide;

N-[2-amino-5-(2-thienyl)phenyl]-1-(3,4,5-trimethoxybenzyl)indoline-6-carboxamide;

trans-*N*-[2-amino-5-(2-thienyl)phenyl]-3-(4-{[(3,4,5-trimethoxyphenyl)amino]methyl}phenyl)acrylamide;

N-[2-amino-5-(2-thienyl)phenyl]-4-{[(3-fluoro-4-methoxyphenyl)amino]methyl}benzamide;

N-[2-amino-5-(2-thienyl)phenyl]-4-{[(6-chloro-5-fluoro-1*H*-benzimidazol-2-yl)thio]methyl}benzamide;

and a pharmaceutically acceptable salt of any one or more of the foregoing.

33. – 503. (Canceled)

504. (Previously presented) A pharmaceutical composition comprising a compound according to claims 1 and a pharmaceutically acceptable carrier, diluent, or excipient.

505. – 511. (Canceled)